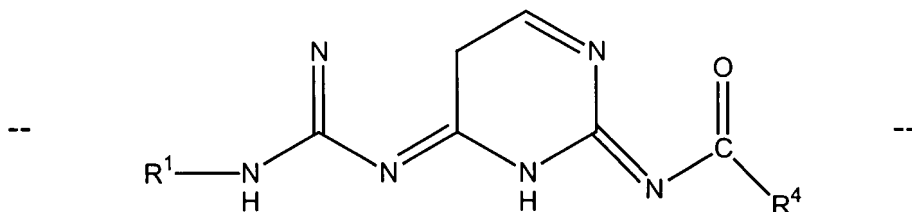


Please add, after the chemical structure and immediately below it:

A¹

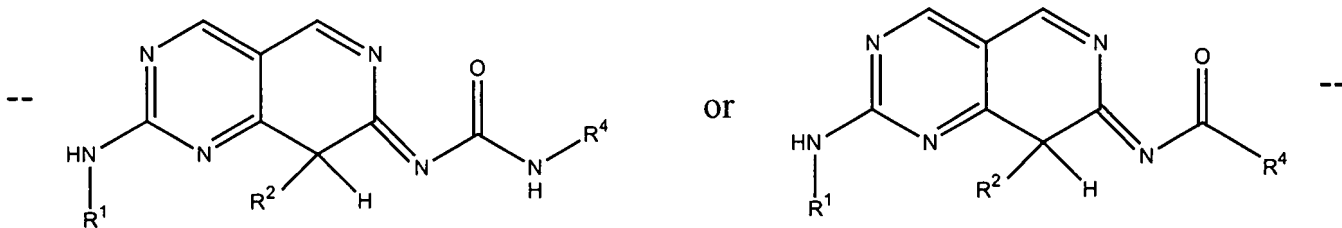
↓ ↑



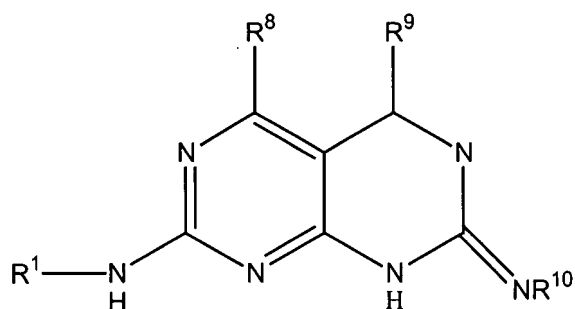
On page 37, after the last two chemical structures, and directly below said structures, please add

↓ ↑

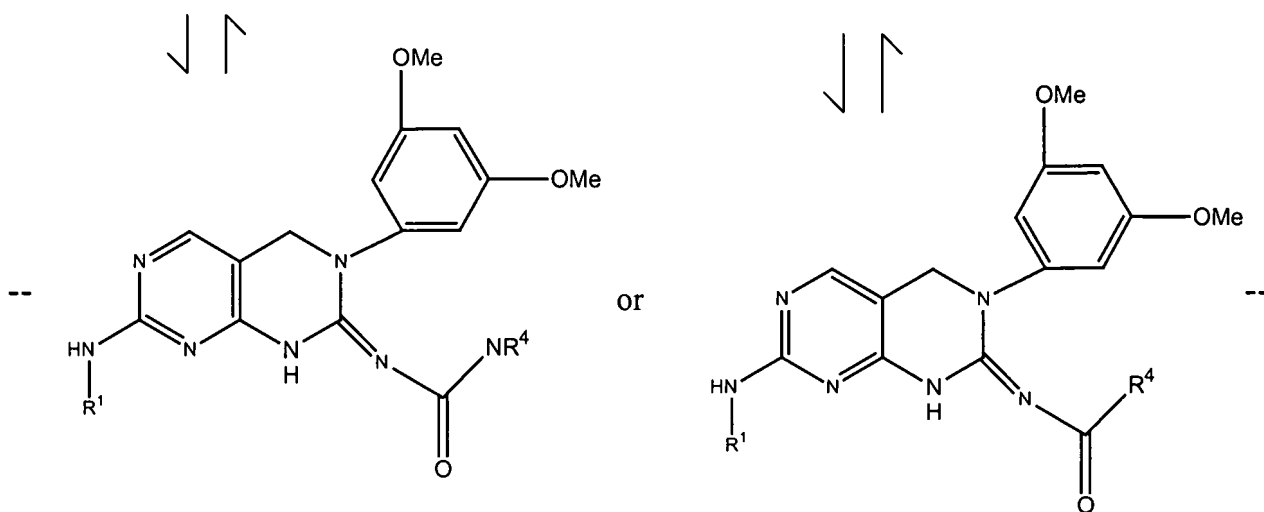
↓ ↑

A²

On page 40, after the chemical structure at line 11, and directly below it, please insert

A³

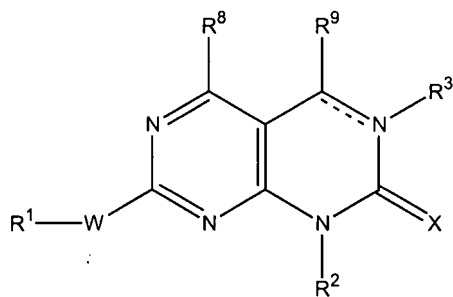
On page 41, after the last two chemical structures, and directly below them, please insert:

A⁴

Please add, as page 132, the Abstract enclosed herewith on a separate sheet.

IN THE CLAIMS:

Claim 1 (amended). A compound of Formula I



I

and the pharmaceutically acceptable salts thereof,

wherein:

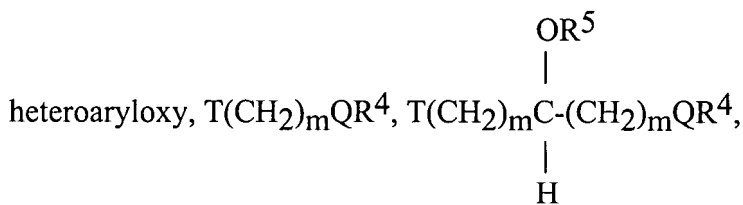
the dotted line represents an optional double bond;

W is NH, S, SO, or SO₂;

X is either O, S, or NR¹⁰;

R¹, R², and R¹⁰ are independently selected from the group consisting of H,

(CH₂)_nAr, COR⁴, (CH₂)_nheteroaryl, (CH₂)_nheterocyclyl, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₂-C₁₀ alkenyl, and C₂-C₁₀ alkynyl, wherein n is 0, 1, 2, or 3, and the (CH₂)_nAr, (CH₂)_nheteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR⁴R⁵, N⁺(O)R⁴R⁵, N⁺R⁴R⁵R⁶Y⁻, alkyl, phenyl, substituted phenyl, (CH₂)_nheteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR⁴, CO₂R⁴, CONR⁴R⁵, SO₂NR⁴R⁵, SO₃R⁴, PO₃R⁴, aldehyde, nitrile, nitro,



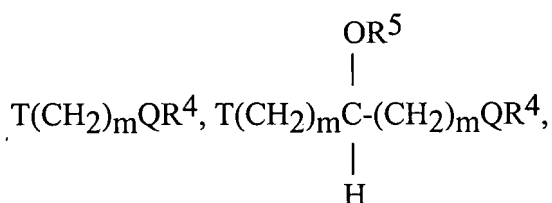
C(O)T(CH₂)_mQR⁴, NHC(O)T(CH₂)_mQR⁴, T(CH₂)_mC(O)NR⁴NR⁵, or T(CH₂)_mCO₂R⁴ wherein each m is independently 1-6, T is O, S, NR⁴,

$N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5 , and Q is O, S, NR^5 , $N^+(O)R^5$, or $N^+R^5R^6Y^-$;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2 , wherein R^2 is as defined above, as well as

OH, NR^4R^5 , $COOR^4$, OR^4 , $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 , PO_3R^4 ,



wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of

hydrogen, C_1 - C_6 alkyl, substituted alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl,

$N(C_1$ - C_6 alkyl)₁ or 2, $(CH_2)_n$ Ar, C_3 - C_{10} cycloalkyl, heterocyclyl, and

heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4 , NR^4R^5 , $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T-(CH_2)_mQR^4$, $CO-T-(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T-(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$.

R^6 is alkyl;

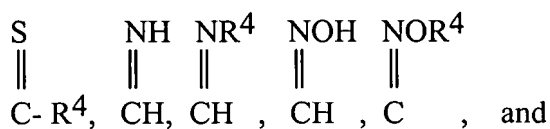
R^8 and R^9 independently are H, C_1 - C_3 alkyl, NR^4R^5 , $N^+(O)R^4R^5$,

$N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4 , CO_2R^4 ,

$CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 , PO_3R^4 , CHO, CN, or NO_2 ;

when the dotted line is absent, R^9 is additionally oxo,

AS
Cont

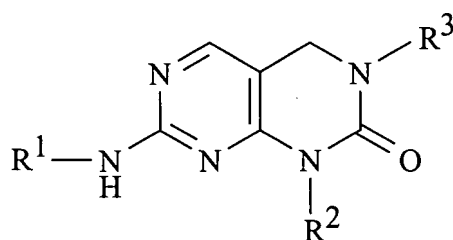


Y is a halo counter-ion.

Claim 2 (amended). A compound of Claim 1 wherein W is NH, and R⁸, and R⁹ both are hydrogen.

Claim 7 (amended). A compound of Claim 2 having the formula

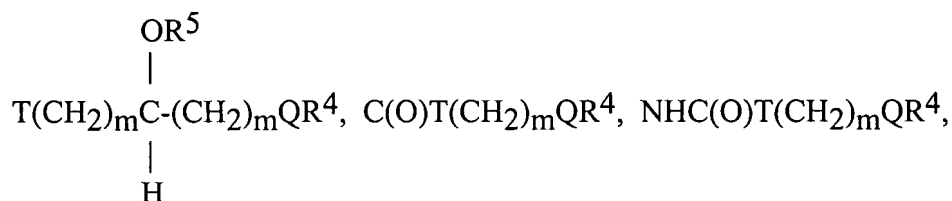
A6



wherein:

R¹, R² and R³ independently are hydrogen, C₁-C₁₀ alkyl, (CH₂)_nAr, (CH₂)_nheteroaryl, C₃-C₁₀ cycloalkyl, (CH₂)_n C₃-C₁₀ cycloalkyl, or (CH₂)_nheteroaryl,

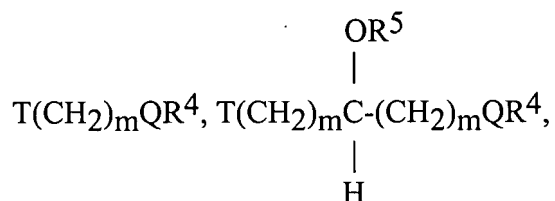
wherein n is 0, 1, 2 or 3, and the (CH₂)_nAr, (CH₂)_nheteroaryl, alkyl, cycloalkyl and heterocyclyl groups are optionally substituted by up to 5 groups selected from NR⁴R⁵, N⁺(O)R⁴R⁵, N⁺R⁴R⁵R⁶Y⁻, alkyl, phenyl, substituted phenyl, (CH₂)_nheteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR⁴, CO₂R⁴, CONR⁴R⁵, SO₂NR⁴R⁵, SO₃R⁴, PO₃R⁴, aldehyde, nitrile, nitro, heteroaryloxy, T(CH₂)_mQR⁴,



$T(CH_2)_mC(O)NR^4NR^5$, or $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4 , $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5 , and Q is O, S, NR^5 , $N^+(O)R^5$, or $N^+R^5R^6Y^-$;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2 , wherein R^2 is as defined above, as well as OH, NR^4R^5 , $COOR^4$, OR^4 , $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 , PO_3R^4 ,



wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1 - C_6 alkyl, substituted alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, $N(C_1$ - C_6 alkyl)₁ or 2, $(CH_2)_nAr$, C_3 - C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

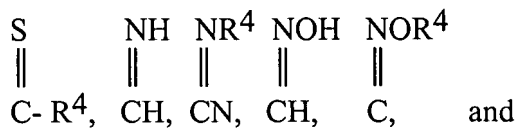
when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4 , NR^4R^5 , $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T-(CH_2)_mQR^4$, $CO-T-(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T-(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

A6
Cont

R^8 and R^9 independently are H, C_1 - C_3 alkyl, NR^4R^5 , $N^+(O)R^4R^5$,
 $N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4 , CO_2R^4 ,
 $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 , PO_3R^4 , CHO, CN, or NO_2 ;

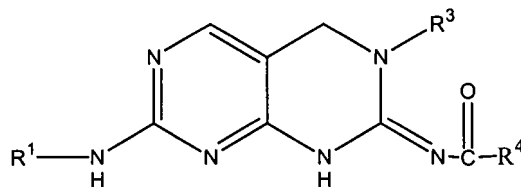
when the dotted line is absent, R^9 is additionally oxo,



Y is a halo counter-ion.

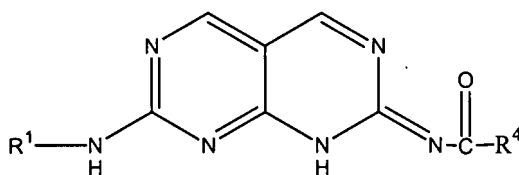
A7

Claim 10 (amended). A compound of Claim 2 having the formula



A8

Claim 12 (amended). A compound of Claim 2 having the formula



Claim 17 (cancelled).

Claim 18 (cancelled).

Claim 19 (cancelled).

Claim 20 (cancelled).

Claim 21 (cancelled).

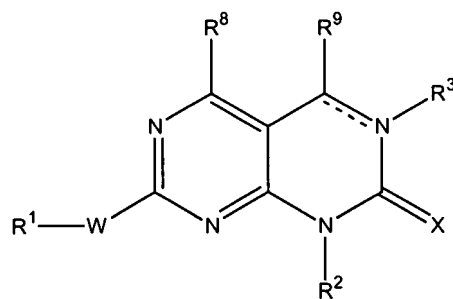
Claim 22 (cancelled).

Claim 23 (cancelled).

Claim 24 (cancelled).

Claim 25 (cancelled).

Claim 26 (amended). A method of inhibiting a cyclin-dependent kinase comprising contacting the cyclin-dependent kinase with a compound of Formula I



and the pharmaceutically acceptable salts thereof,

wherein:

the dotted line represents an optional double bond;

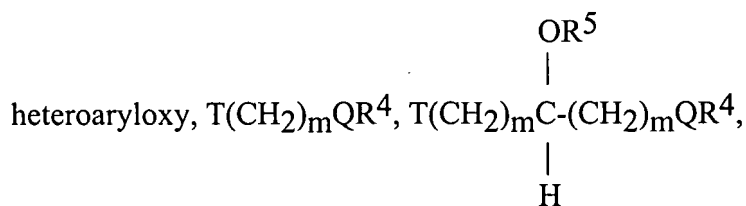
W is NH, S, SO, or SO₂;

X is either O, S, or NR¹⁰;

R¹, R², and R¹⁰ are independently selected from the group consisting of H,

(CH₂)_nAr, COR⁴, (CH₂)_nheteroaryl, (CH₂)_nheterocyclyl, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₂-C₁₀ alkenyl, and C₂-C₁₀ alkynyl, wherein n is 0, 1, 2, or 3, and the (CH₂)_nAr, (CH₂)_nheteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected

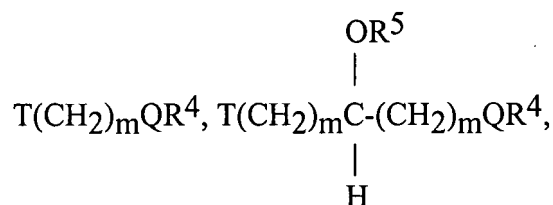
from NR^4R^5 , $\text{N}^+(\text{O})\text{R}^4\text{R}^5$, $\text{N}^+\text{R}^4\text{R}^5\text{R}^6\text{Y}^-$, alkyl, phenyl, substituted phenyl, $(\text{CH}_2)_n$ heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4 , CO_2R^4 , CONR^4R^5 , $\text{SO}_2\text{NR}^4\text{R}^5$, SO_3R^4 , PO_3R^4 , aldehyde, nitrile, nitro,



$\text{C}(\text{O})\text{T}(\text{CH}_2)_m\text{QR}^4$, $\text{NHC}(\text{O})\text{T}(\text{CH}_2)_m\text{QR}^4$, $\text{T}(\text{CH}_2)_m\text{C}(\text{O})\text{NR}^4\text{NR}^5$, or $\text{T}(\text{CH}_2)_m\text{CO}_2\text{R}^4$ wherein each m is independently 1-6, T is O , S , NR^4 , $\text{N}^+(\text{O})\text{R}^4$, $\text{N}^+\text{R}^4\text{R}^6\text{Y}^-$, or CR^4R^5 , and Q is O , S , NR^5 , $\text{N}^+(\text{O})\text{R}^5$, or $\text{N}^+\text{R}^5\text{R}^6\text{Y}^-$;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2 , wherein R^2 is as defined above, as well as OH , NR^4R^5 , COOR^4 , OR^4 , CONR^4R^5 , $\text{SO}_2\text{NR}^4\text{R}^5$, SO_3R^4 , PO_3R^4 ,



wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1 - C_6 alkyl, substituted alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, $\text{N}(\text{C}_1$ - C_6 alkyl)₁ or 2, $(\text{CH}_2)_n\text{Ar}$, C_3 - C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from

AG

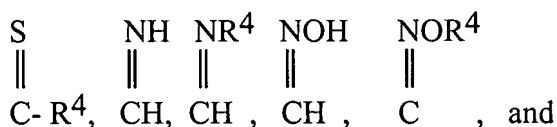
Cont

OH, OR⁴, NR⁴R⁵, (CH₂)_mOR⁴, (CH₂)_mNR⁴R⁵, T-(CH₂)_mQR⁴,
CO-T-(CH₂)_mQR⁴, NH(CO)T(CH₂)_mQR⁴, T-(CH₂)_mCO₂R⁴, or
T(CH₂)_mCONR⁴R⁵;

R⁶ is alkyl;

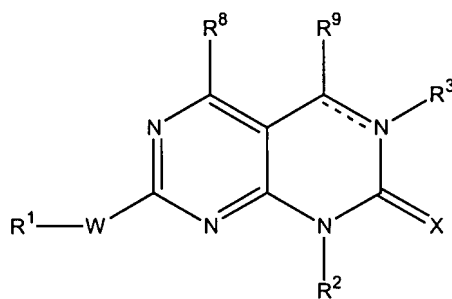
R⁸ and R⁹ independently are H, C₁-C₃ alkyl, NR⁴R⁵, N⁺(O)R⁴R⁵,
N⁺R⁴R⁵R⁶Y⁻, hydroxy, alkoxy, thiol, thioalkyl, halo, COR⁴, CO₂R⁴,
CONR⁴R⁵, SO₂NR⁴R⁵, SO₃R⁴, PO₃R⁴, CHO, CN, or NO₂;

when the dotted line is absent, R⁹ is additionally oxo,



Y is a halo counter-ion.

Claim 30 (amended). A method of inhibiting a growth factor-mediated tyrosine kinase comprising contacting said growth factor-mediated kinase with a compound of Formula I



I

and the pharmaceutically acceptable salts thereof,
wherein:

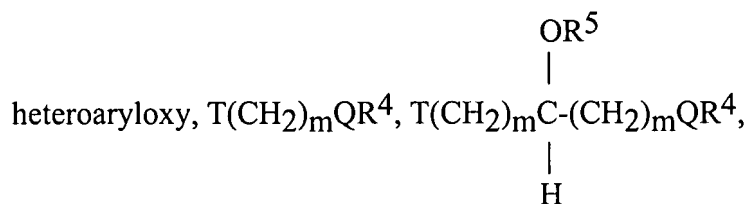
the dotted line represents an optional double bond;

W is NH, S, SO, or SO₂;

X is either O, S, or NR¹⁰;

R^1 , R^2 , and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4 , $(CH_2)_n$ heteroaryl, $(CH_2)_n$ heterocyclyl, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_2 - C_{10} alkenyl, and C_2 - C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$ heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5 , $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$ heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4 , CO_2R^4 , $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 , PO_3R^4 , aldehyde, nitrile, nitro,

A¹⁰
cont

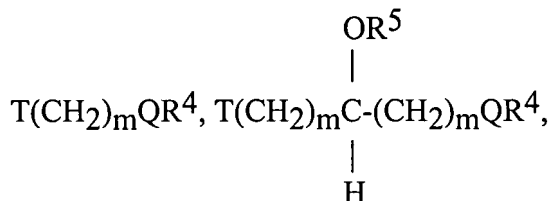


$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, or $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4 , $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5 , and Q is O, S, NR^5 , $N^+(O)R^5$, or $N^+R^5R^6Y^-$;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2 , wherein R^2 is as defined above, as well as

OH, NR^4R^5 , $COOR^4$, OR^4 , $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 , PO_3R^4 ,



wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of

hydrogen, C_1 - C_6 alkyl, substituted alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl,

$N(C_1$ - C_6 alkyl)₁ or 2, $(CH_2)_nAr$, C_3 - C_{10} cycloalkyl, heterocyclyl, and

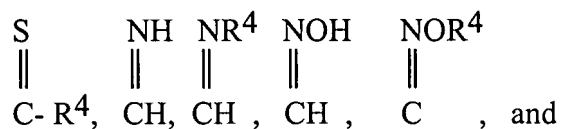
heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH , OR^4 , NR^4R^5 , $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T-(CH_2)_mQR^4$, $CO-T-(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T-(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

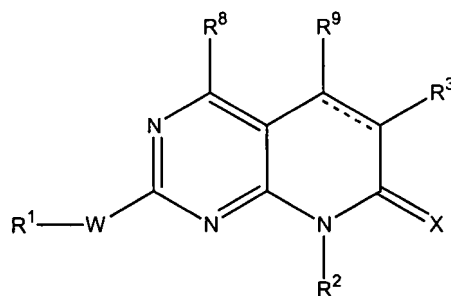
R^8 and R^9 independently are H , C_1 - C_3 alkyl, NR^4R^5 , $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4 , CO_2R^4 , $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 , PO_3R^4 , CHO , CN , or NO_2 ;

when the dotted line is absent, R^9 is additionally oxo,



Y is a halo counter-ion.

Claim 34 (amended). A method of inhibiting a non-receptor tyrosine kinase comprising contacting said non-receptor tyrosine kinase with a compound of Formula I



I

and the pharmaceutically acceptable salts thereof,

wherein:

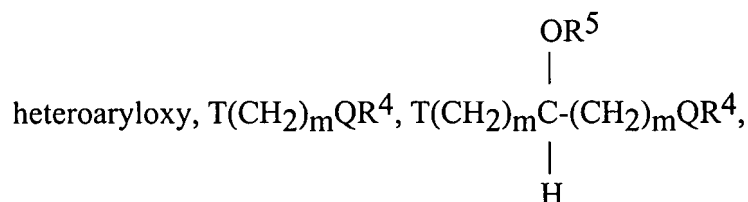
the dotted line represents an optional double bond;

W is NH, S, SO, or SO₂;

X is either O, S, or NR¹⁰;

R¹, R², and R¹⁰ are independently selected from the group consisting of H,

(CH₂)_nAr, COR⁴, (CH₂)_nheteroaryl, (CH₂)_nheterocyclyl, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₂-C₁₀ alkenyl, and C₂-C₁₀ alkynyl, wherein n is 0, 1, 2, or 3, and the (CH₂)_nAr, (CH₂)_nheteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR⁴R⁵, N⁺(O)R⁴R⁵, N⁺R⁴R⁵R⁶Y⁻, alkyl, phenyl, substituted phenyl, (CH₂)_nheteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR⁴, CO₂R⁴, CONR⁴R⁵, SO₂NR⁴R⁵, SO₃R⁴, PO₃R⁴, aldehyde, nitrile, nitro,



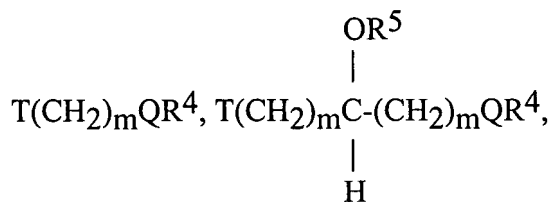
C(O)T(CH₂)_mQR⁴, NHC(O)T(CH₂)_mQR⁴, T(CH₂)_mC(O)NR⁴NR⁵, or T(CH₂)_mCO₂R⁴ wherein each m is independently 1-6, T is O, S, NR⁴, N⁺(O)R⁴, N⁺R⁴R⁶Y⁻, or CR⁴R⁵, and Q is O, S, NR⁵, N(O)R⁵, or NR⁵R⁶Y;

when the dotted line is present, R³ is absent;

otherwise R³ has the meanings of R², wherein R² is as defined above, as well as

OH, NR⁴R⁵, COOR⁴, OR⁴, CONR⁴R⁵, SO₂NR⁴R⁵, SO₃R⁴, PO₃R⁴,

Aⁿ
cont



wherein T and Q are as defined above;

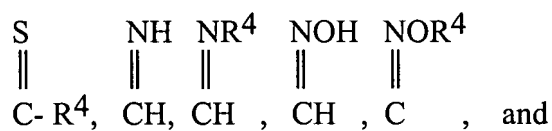
A¹¹
cont
 R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1 - C_6 alkyl, substituted alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, $N(C_1$ - C_6 alkyl)₁ or 2, $(CH_2)_n$ Ar, C_3 - C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4 , NR^4R^5 , $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T-(CH_2)_mQR^4$, $CO-T-(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T-(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, C_1 - C_3 alkyl, NR^4R^5 , $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4 , CO_2R^4 , $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 , PO_3R^4 , CHO, CN, or NO_2 ;

when the dotted line is absent, R^9 is additionally oxo,



Y is a halo counter-ion.

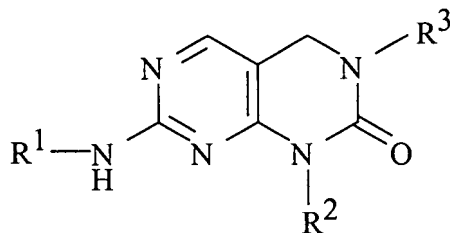
A¹² Claim 37 (amended). A method of treating a subject suffering from vascular smooth muscle cell proliferation comprising administering to said subject a therapeutically effective amount of a compound of Claim 1.

Claim 38 (cancelled).

Claim 40 (cancelled).

Please add new Claims 44-53:

Claim 44 (new). A compound of the formula



wherein:

R¹ is C₁-C₁₀ alkyl or (CH₂)_nAr;

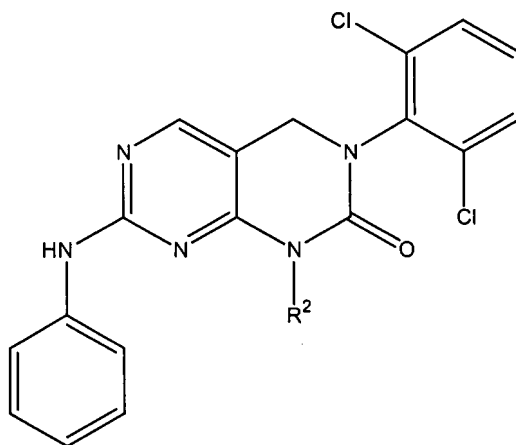
R² is H, C₁-C₁₀ alkyl, or (CH₂)_nAr; and

R³ is Ar,

wherein n is 0, 1, 2 or 3;

Ar is phenyl or phenyl substituted with one or two groups selected from halo, alkyl, or substituted alkyl; or a pharmaceutically acceptable salt thereof.

Claim 45 (new). A compound of the formula



wherein R^2 is $(CH_2)_nAr$, n is 0, 1, 2 or 3, and Ar is phenyl or phenyl substituted by a 2-aminoethyl group,
or a pharmaceutically acceptable salt thereof.

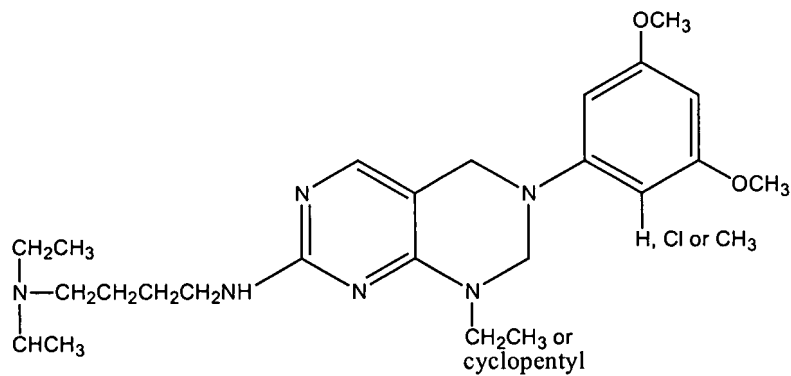
Claim 46 (new). A pharmaceutical formulation comprising a compound of Claim 3 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 47 (new). A pharmaceutical formulation comprising a compound of Claim 7 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 48 (new). A pharmaceutical formulation comprising a compound of Claim 44 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 49 (new). A pharmaceutical formulation comprising a compound of Claim 45 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 50 (new). A compound of the formula



or a pharmaceutically acceptable salt thereof.

Claim 51 (new). The compound 7-(4-diethylamino-butylamino)-3-(2-chloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidine-2(1*H*)-one.

Claim 52 (new). The compound 7-(4-diethylamino-butylamino)-3-(2-methyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidine-2(1*H*)-one.

Claim 53 (new). The compound 7-(4-diethylamino-butylamino)-3-(3,5-dimethoxy-phenyl)-1-cyclopentyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidine-2(1*H*)-one.